Existence of automaticity in anomalous bu. of Wolff-Parkinson-White syndrome[1]

JULIO PRZYBYLSKI, PABLO A. CHIALE, M. SUSANA HALPERN, JULIO O. LÁZZARI, MARCELO V. ELIZARI, AND MAURICIO B. ROSENBAUM

From the Service of Cardiology, Ramos Mejia Hospital, Buenos Aires, Argentina

SUMMARY Escape beats probably arising from the anomalous bundle were documented in 2 patients with the Wolff-Parkinson-White (WPW) syndrome. A third patient, in whom complete AV block developed both in the anomalous bundle and the normal pathway, showed the occurrence of escape beats (an escape-bigeminy pattern), as well as a regular idioventricular rhythm arising from the anomalous bundle. Phase 4 block in the anomalous bundle occurred in 7 other patients, in 4 of them spontaneously and in 3 only after the administration of ajmaline or amiodarone. Only 4 of 14 fully investigated patients (out of a total number of 23) showed absence of both escape beats and phase 4 block.

The escape beats were considered as direct evidence, and the phase 4 block as indirect evidence, for the existence of automaticity in the anomalous bundle. Such evidence supports the view that the anomalous bundle, like the His bundle-branch system, may be composed of specialised tissue endowed with the property of automaticity.

Over the past 10 years, a large number of studies have indicated that the Wolff-Parkinson-White (WPW) syndrome is related to the existence of an anomalous bundle (also referred to as the Kent bundle), which directly connects atrial with ventricular tissue, bypassing the normal atrioventricular (AV) junction (Boineau and Moore, 1970; Wallace *et al.*, 1971). Attempts have been made to delineate the physiological properties of the anomalous bundle (Castellanos *et al.*, 1970; Roelandt *et al.*, 1970). It has been shown that the anomalous bundle operates as a conducting fascicle which can transmit impulses bidirectionally at a great speed (Burchell *et al.*, 1967; Wellens and Durrer, 1974); the duration of refractoriness in the anomalous bundle has also been determined (Durrer *et al.*, 1967; Lau *et al.*, 1972; Wellens and Durrer, 1973; Gilbert *et al.*, 1975). However, the anatomical nature of the anomalous bundle is still under debate (Wood *et al.*, 1943; Lev, 1966; James, 1970; Anderson *et al.*, 1974; James and Puech, 1974), and there is very little information regarding the existence or absence of automaticity in the Kent bundle (Pick and Katz,

1955). In this paper, evidence will be presented suggesting that the anomalous bundle, like other normal or diseased conducting fascicles of the human heart, is also endowed with the property of automaticity. This may have a bearing on the anatomical structure of the Kent bundle.

Subjects and methods

Twenty-three patients with the WPW syndrome were studied. Table 1 shows the age and sex of the patients, type of WPW, the nature of tachyarrhythmias if present, and any associated cardiac disease. The main purpose of the study was to show the presence of phase 4 block in the anomalous bundle and/or escape beats arising from it, and in order to achieve this, the sinoatrial rate was slowed as much as possible by carotid sinus massage in 21 patients. In the other 2 patients, either phase 4 block or escape beats arising from the anomalous bundle occurred spontaneously. Carotid sinus massage was repeated in 12 of the 23 patients 5 to 10 minutes after the intravenous injection of 50 mg of ajmaline, and in 15 patients during oral administration of amiodarone (200 to 600 mg/day). These 'conduction-depressing drugs' are known to increase the phase 4 block range (Chiale *et al.*, 1975;

Table 1 *Clinical features of 23 patients with WPW syndrome*

Case No.	Age (y and sex)		WPW type	Tachyarrhythmias	Clinical diagnosis
1	42	M	A	—	Chronic Chagasic myocarditis
2	45	M	A	—	Systemic hypertension
3	61	M	A	—	Systemic hypertension, diabetes, alcoholism
4	60	M	A	PST	—
5	39	M	A	PST	—
6	46	M	A	PST	—
7	51	M	A	—	Systemic hypertension
8	61	M	B	—	—
9	58	F	B	—	—
10	65	M	A	AT with AV block*	Chronic cor pulmonale
11	71	M	B	—	Ischaemic heart disease, systemic hypertension
12	66	M	B	PAF, PST	Ischaemic heart disease
13	45	M	A	PST	—
14	32	M	A	PST	—
15	57	M	A	PAF	—
16	21	M	B	PST	—
17	30	F	B	PST	—
18	58	F	A	PST	Systemic hypertension
19	17	F	B	PST	Ebstein's disease
20	17	M	A	—	—
21	32	F	A	PST, PAFl	—
22	54	F	A	PST	—
23	33	F	A	PST	Mitral stenosis

*Atrial tachycardia with high degree of block in both AV node and anomalous bundle.
Abbreviations: AT, atrial tachycardia; PST, paroxysmal supraventricular tachycardia; PAF, paroxysmal atrial fibrillation; PAFl, paroxysmal atrial flutter.

Rosenbaum, 1974). In 2 patients (cases 1 and 2), His bundle electrograms were recorded during the manoeuvres described above.

Phase 4 block (bradycardia-dependent) was assumed to occur whenever conduction in the anomalous bundle was interrupted or absent after relatively long diastolic intervals. Phase 3 block (tachycardia-dependent), which commonly accompanied phase 4 block, was assumed to occur whenever conduction in the anomalous bundle was interrupted or absent after relatively short diastolic intervals. Obviously, block in the anomalous bundle expresses itself by normalisation of the QRS and disappearance of the WPW aberrancy, in contrast with block in the bundle-branches which causes an abnormal or aberrant QRS. The occurrence of phase 3 and phase 4 block ranges separating an intermediate normal conduction range in the anomalous bundle was determined when possible, and depicted diagrammatically as previously described for patients with intermittent bundle-branch block (BBB) (Elizari *et al.*, 1972; García and Rosenbaum, 1972; Rosenbaum *et al.*, 1973a, b) (see Fig. 3). This usually required the analysis of 500 to 1000 beats from a single long tracing, during which different diastolic intervals were provoked (Elizari *et al.*, 1972; García and Rosenbaum, 1972; Rosenbaum *et al.*, 1973a, b). Since phase 4 block has been related to the existence of phase 4 depolarisation (Singer *et al.*, 1967; Rosenbaum *et al.*, 1973a, b), its presence in the anomalous bundle was taken as *indirect* evidence for normal or en-

hanced automaticity in the Kent bundle. Beats which were not preceded by a P wave, showed the same QRS configuration as sinus beats with WPW or a greater degree of pre-excitation, and had a constant coupling interval, were interpreted as escape beats arising from the anomalous bundle. When present, these were taken as *direct* evidence for the existence of automaticity in the anomalous bundle.

Results

Only 9 of the 23 patients showed diastolic intervals of 2000 ms or longer, and this was set as an arbitrary limit for inclusion in the final study, though much longer intervals are sometimes needed to uncover the presence of phase 4 block or escape beats. In 5 other cases, either phase 4 block or escape beats arising from the anomalous bundle occurred after diastolic intervals shorter than 2000 ms. Thus, 14 cases were selected for analysis (summarised in Table 2). Phase 4 block in the anomalous bundle occurred in 7 of the 14 patients, in 4 of them spontaneously and in 3 only after administration of ajmaline or amiodarone. Escape beats arising from the anomalous bundle occurred in 3 other patients. Only 4 of the 14 patients showed neither phase 4 block nor escape beats.

ESCAPE BEATS AND IDIOVENTRICULAR
RHYTHM ARISING FROM ANOMALOUS BUNDLE
In one patient (case 12), escape beats arising from

Table 2   *Phase 4 block and escape beats arising from anomalous bundle before and after administration of drugs*

Case No.	Control Phase 4 block	Escape beats	Ajmaline IV Phase 4 block	Escape beats	Amiodarone oral Phase 4 block	Escape beats
1	*	—	Yes	—	Yes	—
2	—	—	Yes	—	Yes	?Concealed†
3	Yes	—				
4	—	—			—	—
5	—	—			—	—
6	—	—	—	—	—	—
7	—	—	—	—	—	—
8	Yes	?Concealed†	Rate independent block in anomalous bundle			
9	Yes	—				
10	—	Yes				
11	—	Yes				
12	—	—				Yes
13	Yes	—				
14	—	—	Yes	—		

*No evidence.
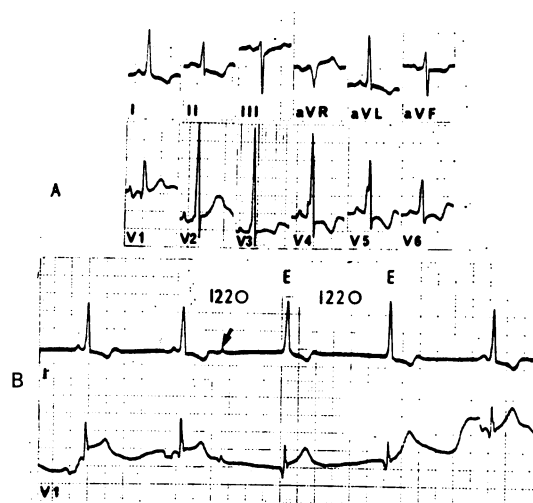† ? concealed escape beats arising in anomalous bundle (see text).

Fig. 1   *Case 11. A. Electrocardiogram showing WPW pattern. B. Leads I and VI recorded simultaneously during carotid sinus massage showing escape beats (E) arising from the anomalous bundle. Arrow shows blocked atrial ectopic beat (see text for further description).*

the anomalous bundle were recorded during carotid sinus stimulation after pauses of 2060 ms, but only during administration of amiodarone. In another patient (case 11), escape beats arising from an anomalous bundle occurred in the absence of drugs (Fig. 1). In Fig. 1 B, after two sinus beats conducted through the anomalous bundle and showing a WPW pattern, a premature atrial beat (arrow) is blocked both in the AV node (because of the vagal stimulation) and in the anomalous bundle (indicating phase 3 block in the latter). After this, two consecutive escape beats occur, not preceded by P waves, with an escape interval of 1220 ms, and showing

a similar QRS pattern to that of the sinus beats. These are assumed to arise from the anomalous bundle. The larger delta wave indicates that ventricular activation depends upon the impulse arriving from the anomalous bundle, with little or no participation of the normal pathway, as is to be expected from a beat arising from the anomalous bundle.

The most interesting of these three cases was the one illustrated in Fig. 2. This was a 65-year-old man (case 10) with chronic cor pulmonale and congestive heart failure, who was fully digitalised. At a particular moment, he developed high grade block both in the anomalous bundle and in the normal pathway, the latter probably caused or enhanced by digitalis. Strip A in Fig. 2 was recorded during an episode of atrial tachycardia at a rate of 166 per minute, and shows absence of conduction over the normal pathway, and second degree AV block (Mobitz type II) in the anomalous bundle. Strip B was recorded when the atrial rate was about 187 per minute and shows, in the presence of a higher degree of AV block, a typical escape bigeminy distribution of WPW beats. The escape beats (E) occur after a constant coupling interval of 960 ms, show the same WPW pattern of the atrial conducted beats, and are not immediately preceded by P waves, thus fulfilling all the criteria for escape beats arising from the anomalous bundle. The conducted beats (C) can actually be considered as captures occurring through the anomalous bundle. (Since the normal pathway was completely blocked, the QRS showed total pre-excitation both during the conducted and escape beats.) Strip C illustrates a period of complete AV dissociation, with an idioventricular rhythm at a rate of 62 beats per minute, showing the same WPW configuration (RR interval 960 ms). This fulfils the criteria for an
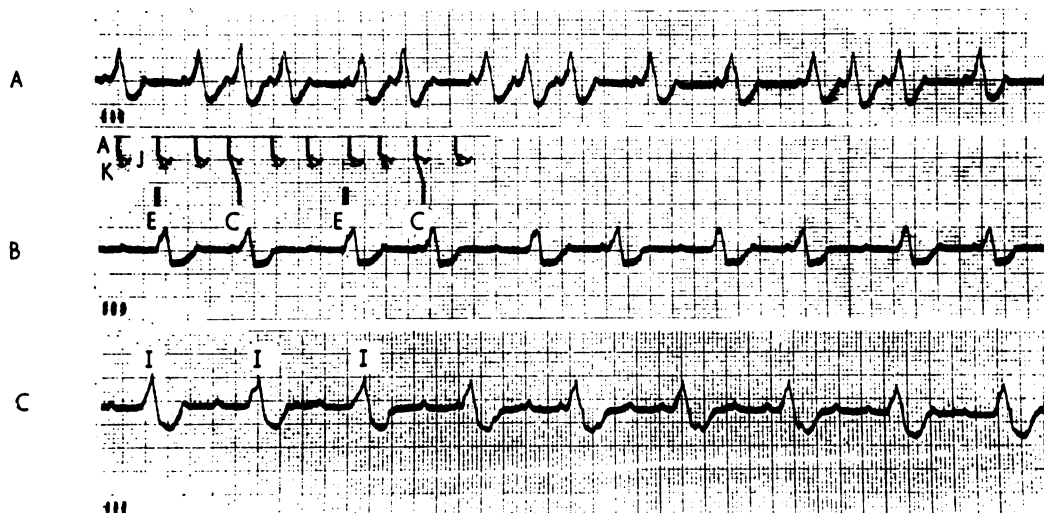
Fig. 2 *Case 10. Lead III. Escape beats (E) and idioventricular rhythm (I) arising from the anomalous bundle.*
Strip A shows atrial tachycardia complete block in the normal pathway, and Mobitz type II block in the
anomalous bundle. Strip B shows atrial tachycardia, complete block in the normal pathway, high grade block in the
anomalous bundle, escape beats arising from the anomalous bundle (E) with a constant escape interval of 960 ms,
and capture beats (C) through the anomalous bundle. The 'delta-P' interval of the capture beats is 40 ms longer
than that of the blocked P waves preceding the escape beats. Diagrammatic interpretation is shown above.
A, atria; K, Kent bundle; J, normal pathway; V, ventricles. Strip C, recorded a few days later, shows complete
block both in the normal and anomalous pathways, with an idioventricular rhythm (I) arising from the anomalous
bundle with an interectopic interval of 960 ms, similar to the escape interval in strip B (for further description
see text).

idioventricular rhythm arising from the anomalous bundle. The relatively rapid rate of this ectopic rhythm is similar to that which one would expect from the His bundle.

PHASE 4 BLOCK IN ANOMALOUS BUNDLE
Fig. 3 illustrates the 7 patients in whom phase 4 block (and also phase 3 block) in the anomalous bundle was documented. In the first 4 cases (3, 8, 9 and 13), phase 4 block in the anomalous bundle occurred spontaneously during the long pauses caused by carotid sinus massage (in 1 of these 4 patients, phase 4 block occurred spontaneously after postextrasystolic pauses). In the last 3 cases (cases 1, 2, and 14), phase 4 block in the anomalous bundle was uncovered only by ajmaline or amiodarone. It is apparent that in all 7 patients, except case 3, phase 3 block in the anomalous bundle was also present. One of the cases in which phase 3 and phase 4 block in the anomalous bundle occurred spontaneously is illustrated in Fig. 4. The occurrence of phase 3 and phase 4 block ranges separating an intermediate normal conduction range in the anomalous bundle gives rise to the same kind of 'accordion effect' previously described in patients

with intermittent bundle-branch block (Elizari *et al.*, 1972; García and Rosenbaum, 1972; Rosenbaum *et al.*, 1973a, b). Fig. 5 illustrates one of the cases in which phase 3 and phase 4 block in the anomalous bundle could be documented only after ajmaline. These observations show the physiological similarity between the spontaneously occurring and the drug-induced conduction disturbances in the anomalous bundle.

In the patients in whom phase 4 block occurred spontaneously, the administration of ajmaline or amiodarone caused a definite shift of the phase 4 block range to the left, at the expense of the normal conduction range. This suggests that, when these drugs appeared to cause phase 4 block in the anomalous bundle to occur apparently as a new phenomenon, their effect was to shift a pre-existing but late phase 4 block range to the left. In fact, an extremely late phase 4 block range, which cannot be documented because extremely long diastolic pauses (impossible to obtain in the human) are needed, can only be uncovered under the action of these drugs which depress conduction. However, the possibility that these drugs may actually induce phase 4 block cannot be totally dismissed. Whether
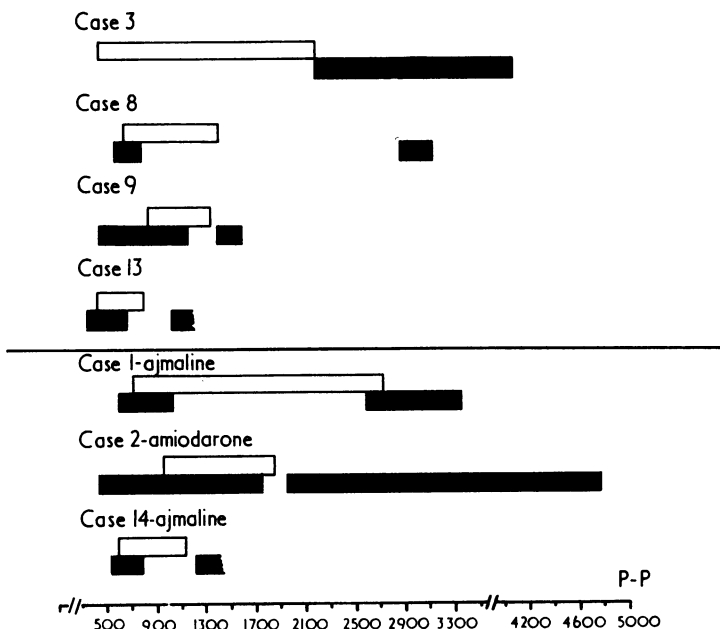
Fig. 3 *Diagrammatic display of the presence of phase 4 and phase 3 block in 7 patients with WPW syndrome. Black bars to the left denote phase 3 block in the anomalous bundle; black bars to the right, phase 4 block in the anomalous bundle; and white bars, normal conduction in the anomalous bundle. Bottom scale: PP intervals in ms. In the upper 4 cases, the conduction disturbances in the anomalous bundle occurred spontaneously, in the lower 3 cases only with ajmaline or amiodarone. This diagram is similar to the one originally employed to describe intermittent bundle-branch block (Elizari et al., 1972; Garcia and Rosenbaum, 1972; Rosenbaum et al., 1973a, b).*
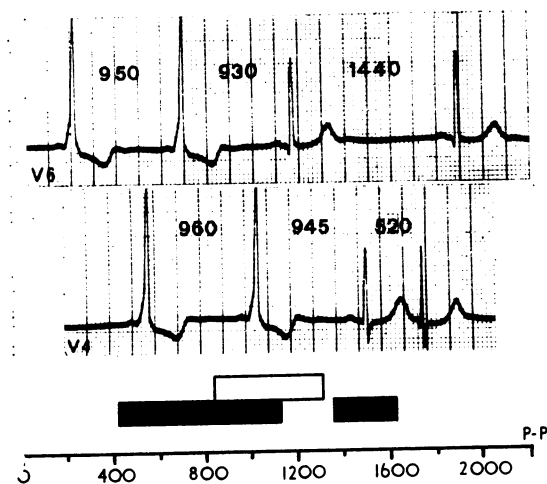

Fig. 4 *Case 9. Rate-dependent block in the anomalous bundle. PP intervals are indicated in ms. Diagram (as in Fig. 3) based on analysis of 650 beats from a single long tracing. In the upper electrocardiographic record, the pause of 1440 ms was caused by a blocked atrial extrasystole falling on the T wave of the preceding beat. In the lower record, the fourth beat is a premature supraventricular beat, with slightly aberrant intraventricular conduction. Thus, the WPW configuration, which indicates normal conduction in the anomalous bundle, occurs only after diastolic intervals of intermediate length, whereas a normal QRS, which indicates block in the anomalous bundle, occurs both after relatively shorter and relatively longer diastolic intervals.*
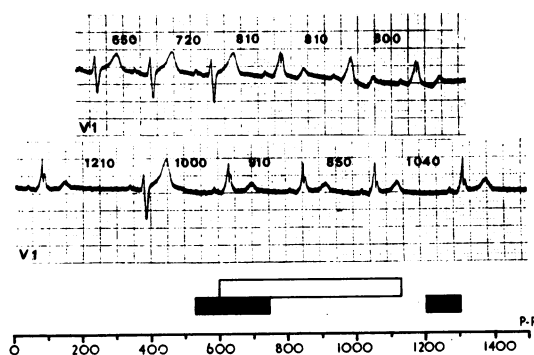

Fig. 5 *Case 14. Rate-dependent block in the anomalous bundle, occurring only after an intravenous injection of of 50 mg ajmaline, during carotid sinus stimulation. In the control study (not shown), similar changes in rate left the WPW pattern unchanged. Symbols and description as in Fig. 4. The diagram was based on the analysis of 952 beats from a single long tracing, from which the electrocardiographic records illustrated were selected.*

or not this is so, the observation of phase 4 block, occurring spontaneously or under the effect of drugs, is indirect evidence for automaticity in the anomalous bundle of patients with the WPW syndrome.

In the upper part of Fig. 6 (case 2), the first three beats show a WPW pattern and the two subsequent
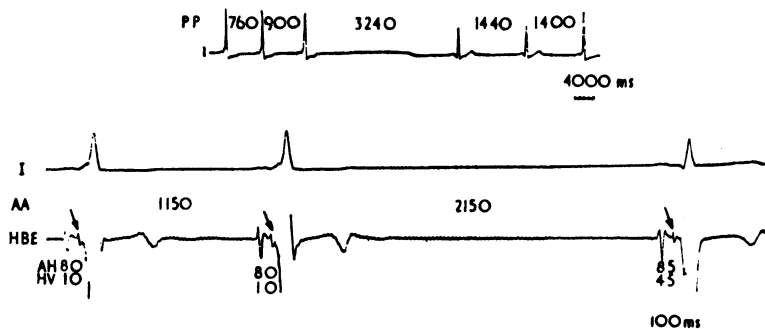
Fig. 6 *Case 2. His bundle electrogram (HBE) recorded from a patient with phase 4 block in the anomalous bundle, as shown by the fourth and fifth beats in the upper electrocardiographic strip (lead I). The HBE shows that, in the third beat, with normal QRS after pause of 2150 ms (indicating phase 4 block in the anomalous bundle), the AH interval is slightly longer than in the first two beats showing a WPW pattern. This indicates that normalisation of the QRS in the third beat was not the result of acceleration of transnodal conduction.*

beats, after diastolic intervals of 3240 and 1440 ms caused by vagal stimulation, show normalisation of the QRS, indicating phase 4 block in the anomalous bundle. The lower part of Fig. 6 shows a similar response during a His bundle recording (HBE). The AH interval is slightly longer in the third beat (after the pause of 2150 ms) showing phase 4 block in the anomalous bundle, than in the first two beats with the WPW pattern, indicating that normalisation of the QRS was not the result of acceleration of conduction in the normal pathway; this further supports the view that phase 4 block in the anomalous bundle was the mechanism responsible. In this patient, and also in case 8, long pauses within the phase 4 block range were terminated on a number of occasions by sinus beats conducted with a WPW pattern, when conduction in the anomalous bundle was unexpected. This paradoxical late conduction through the anomalous bundle may result from the occurrence of concealed escape beats in the anomalous bundle (Rosenbaum *et al.*, 1974; Elizari *et al.*, 1976).

Discussion

In three of the cases presented in this paper, escape beats or an idioventricular rhythm occurred, showing the same WPW pattern as in sinoatrial conducted beats or an increase in the degree of pre-excitation. It is reasonable to assume that these automatic beats arose from the anomalous bundle, particularly in the patient who developed complete AV block (Fig. 2). It may be argued, however, that such automatic beats may arise not in the anomalous bundle itself, but from its atrial or ventricular in-

sertion, but, though this possibility cannot be totally disregarded, it appears unlikely that automatic tissue should exist at the atrial entrance to or the ventricular exit from the anomalous bundle and not in the anomalous bundle itself. This discussion may even be irrelevant in the light of the concept that the anomalous bundle may have its own AV junction which, except for the absence of a node, is similar to the AV junction of the normal AV pathway. It could then be said that the automatic beats in these 3 patients arose from the anomalous bundle atrioventricular junction.

If it is accepted that the anomalous bundle or its junction is endowed with the property of automaticity, the following questions should be asked: Is this a constant or only an occasional feature of the WPW syndrome? Why is it that automaticity in the anomalous bundle seems to be so uncommon? What other properties characterise the anomalous bundle when functioning as an automatic tissue? In this connection, some previous reports deserve careful analysis. In 1955, Pick and Katz postulated that the anomalous bundle was composed of automatic tissue, and presented a case of WPW (their Fig. 5) showing premature systoles initiated by retrograde P waves followed, after a PR interval shorter than that of the sinoatrial beats with WPW, by an 'exaggerated' WPW pattern. The same exaggerated WPW beats occurred also as a regular rhythm at a rate of 75 beats per minute. Katz and Pick concluded that 'The ectopic focus must therefore be localised to an area which permits: (1) rapid retrograde stimulation of the atria; and (2) stimulation of the ventricles over anomalous pathways, either completely when the ectopic focus dominates the

heart, or partially when the sinus rhythm is effective. The logical conclusion is that the ectopic focus is located within an anomalous bridge'. In 1971, Moulopoulos et al. reported a patient with WPW (their case 5, Fig. 7), who shortly after an intravenous injection of 1 mg atropine, developed AV dissociation with preservation of the WPW pattern, a clear indication of a rhythm arising from the anomalous bundle. Though to our knowledge not many similar cases have been reported, it is our feeling from personal experience, that, either spontaneously or after slight vagal stimulation and particularly after the administration of atropine, many patients with the WPW syndrome develop beats or rhythms arising from the anomalous bundle; in some of these the QRS complex is preceded shortly by a retrograde P wave, as in the case reported by Katz and Pick, and in others the P wave is probably buried within the WPW QRS complex, as in the case reported by Moulopoulos et al. The old concept (Wilson, 1915; Rosenbaum et al., 1945) that in the WPW syndrome the development of a junctional rhythm should be accompanied by normalisation of the QRS because the ectopic focus is now closer to the ventricle than to the anomalous bundle, should be supplemented by the additional concept that, when a 'junctional' rhythm occurs with preservation of the WPW pattern and even more so when the WPW configuration is exaggerated, the ectopic focus is located within the anomalous bundle. Our present impression is that, in the same way that the normal pathway and the anomalous bundle compete with each other for transmission of sinus impulses, giving rise to the well-known fusion of normal and anomalous ventricular excitation, the His bundle and the anomalous bundle also compete with each other for pacemaking of the heart when 'junctional' automaticity is enhanced or sinus automaticity is depressed. The fact that automaticity in the anomalous bundle may be enhanced by atropine (and perhaps depressed by strong vagal stimulation) suggests that, like the normal AV junction, the anomalous bundle may also be sensitive to vagal influence.

The fact that phase 4 block in the anomalous bundle was documented in 7 of 14 patients supports the view that the anomalous bundle may be composed of automatic fibres in most if not all patients with WPW syndrome. Phase 4 block cannot occur unless spontaneous diastolic depolarisation occurs in fibres of the involved fascicle, and this is the most representative physiological phenomenon underlying the property of automaticity. In addition, since phase 4 block cannot occur in normal Purkinje fibres (Singer et al., 1967; Rosenbaum et

al., 1973, 1974) the possibility arises that the anomalous bundle may be either normal or diseased, or that conduction in it may be normal or abnormal. Thus, our 7 patients with phase 4 block can be considered to have a diseased or malfunctioning anomalous bundle, and the 4 patients in whom no drug or manoeuvre was capable of altering conduction in the anomalous bundle, can be considered to have a normal or normally functioning anomalous bundle. Thus, a fascinating analogy can be drawn between the anomalous bundle of the WPW syndrome and the His bundle-branch system. Indeed, as shown in the present study, the anomalous bundle may behave physiologically and after pharmacological interventions in the same way as the His bundle and the main bundle-branches. Further reasons, supporting the view that it is possible to distinguish between a normal and a diseased or malfunctioning Kent bundle and that this may have profound prognostic and therapeutic implications, have been discussed in a previous paper (Przybylski et al., 1975).

It is remarkable that, while our 7 patients with phase 4 block did not show escape beats arising in the anomalous bundle, our 3 patients with escape beats did not show phase 4 block. However, the reasons why escape beats do not necessarily occur when phase 4 block can be demonstrated have been extensively discussed elsewhere (Rosenbaum et al., 1974). It was then postulated that 'concealed escapes' may occur in the presence of phase 4 block, as actually seemed to occur in 2 of our 7 cases. In a recent microelectrode study of isolated preparations, direct electrophysiological evidence of the occurrence of concealed escapes in the presence of phase 4 block has been provided (Elizari et al., 1976).

Numerous histological studies (Wood et al., 1943; Deerhake et al., 1947; Levine and Burge, 1948; Truex et al., 1960; Lev et al., 1961; Lev, 1966; Lev et al., 1966; Cole et al., 1970; James, 1970; Rosenberg et al., 1971; Anderson et al., 1974; James and Puech, 1974) have failed to determine the precise anatomical nature of the Kent bundle. Against such a background, the characterisation of the physiological properties of the Kent bundle (Durrer et al., 1967; Castellanos et al., 1970; Roeland et al., 1970; Lau et al., 1972) is very relevant. Thus, the direct and indirect evidence presented in this paper for the existence of automaticity supports the view that the anomalous bundle, like the His bundle-branch system, may be composed of fibres endowed with the property of automaticity. The fact that automatic beats or rhythms may arise from the anomalous bundle and be under vagal influence, strengthens the view that the anomalous bundle can be likened to an 'extra-His

bundle' (Przybylski *et al.*, 1975). Ectopic or automatic beats arising from the anomalous bundle may possibly initiate at least some of the arrhythmias which commonly accompany the WPW syndrome.

A few cases have been reported in which the anomalous bundle was found to be histologically composed of specialised tissue (Verduyn Lunel, 1972; James and Puech, 1974); and it has been postulated that the anomalous bundle may be formed from remnants of the embryonic atrioventricular ring (Anderson *et al.*, 1974) and thus retain the properties of specialised cardiac tissue (Anderson *et al.*, 1975). These findings support our view that the anomalous bundle, like the His bundle-branch system, may develop automaticity at least in some cases of WPW syndrome. An alternative explanation of our observations may be provided by the recent demonstration that severely damaged or partially depolarised working myocardium may also develop spontaneous automatic activity (Solberg *et al.*, 1972; Wit *et al.*, 1974; Noble, 1975). However, since this can only occur in the presence of 'slow response' type of activity which is inconsistent with the rapid conduction which occurs in the anomalous bundle, this second explanation appears less likely.

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Requests for reprints to Dr Mauricio B. Rosenbaum, Service of Cardiology, Ramos Mejía Hospital, Urquiza 609, 1221 Buenos Aires, Argentina.